

1. A method of detecting a target nucleic acid sequence in a sample by contacting the sample with a probe to hybridize the probe to the target sequence, and detecting the hybridized probe, said probe having two free nucleic acid end parts which are at least partially complementary to and capable of hybridizing to two at least substantially neighboring regions of the target sequence, comprising the following steps:

a) hybridizing the target sequence to the probe ends under hybridizing conditions;

b) covalently connecting the ends of the hybridized probe with each other to form a circularized structure;

wherein the probe is provided indirectly or directly with a solid phase anchor (A or A through E) and with a cleavable (B) and a detectable function (C), or a dissociable (D, F) and detectable function (C), in such a way that the detectable function (C) remains linked to the solid phase if the target has interacted with the probe;

and the method comprises the further steps of:

c) cleaving said cleavable function (B) if present;

d) separating detectable functions no longer linked to said solid phase; and

e) detecting the presence and, if desired, location of the remaining probe as indicative of the presence of the target nucleic acid sequence.

2. The method according to claim 1, wherein said detectable function is cleaved by cleaving a cleavable linker located on the same probe end as the detectable function.

3. The method according to claim 1, wherein one or both of the probe ends have at least two branches,

preferably with differential sequence specificities, and a detectable function is provided on each of the branches on one end part of the probe, the detectable functions preferably being different and distinguishable from each other.

4. The method according to claim 3, wherein one probe end is linear and the other probe end is branched, preferably bifurcated.

5. The method according to claim 1, wherein said detectable function is dissociable by being provided on a circular probe hybridizing to said target-specific probe.

6. The method according to claim 1, wherein said detectable function is dissociable by being provided on said target-specific probe hybridizing to a circular probe.

7. The method according to claim 1, wherein said target-specific probe is designed to hybridize to the target molecule to leave an interspace between the probe ends, at least one additional probe is provided which is designed to hybridize to the target molecule in said interspace, and the hybridized probes are covalently interconnected.

8. The method according to claim 1, wherein said target-specific probe or probes are designed to hybridize to the target molecule to leave a small gap between adjacent probe ends, and said gap or gaps are filled by an extension reaction prior to covalently interconnecting the probe ends.

9. The method according to claim 1, wherein said covalent connection of the probe ends is performed by

enzymatic, ribozyme-mediated or chemical ligation, preferably enzymatic ligation.

10. The method according to claim 1, wherein said target molecule is a DNA or RNA sequence.

11. The method according to claim 1, wherein said probe or probes are oligonucleotides.

12. The method according to claim 1, wherein said probe or probes are immobilized to a solid phase.

13. The method according to claim 1, wherein said target sequence is immobilized to a solid phase.

14. A kit for detecting a target nucleic acid sequence in a sample, comprising

a) a probe having two free nucleic acid end parts which are at least partially complementary to and capable of hybridizing to two at least substantially neighboring regions of the target sequence;

b) a means for connecting the ends to each other after hybridization to the target sequence;

wherein

c) the probe is provided indirectly or directly with a solid phase anchor (A or A through E) and with a cleavable (B) and a detectable function (C), or a dissociable (D, F) and detectable function (C); and, optionally,

d) a cleaving agent.

15. The kit according to claim 14, wherein the detectable function is a fluorophore, radioisotope, hapten or enzyme.

16. The kit according to claim 14 wherein one or both of the two free nucleic acid end parts of the probe have at least two branches, preferably with differential sequence specificities, that each of the branches on one end part of the probe is provided with a different detectable function.

17. The kit according to claim 16, wherein one probe end is linear and the other probe end is branched, preferably bifurcated.

18. A method of distinguishing between sequence specific variants of nucleic acids, comprising using a kit according to claim 14.

19. A circularizable probe having two free nucleic acid end parts which are at least partially complementary to and capable of hybridizing to two at least substantially neighboring regions of a target sequence, wherein the probe is provided indirectly or directly with a solid phase anchor (A or A through E) and with a cleavable (B) and a detectable function (C), or a dissociable (D, F) detectable function (C).

20. The probe according to claim 19, wherein one or both of the two free nucleic acid end parts of the probe have at least two branches, preferably with differential sequence specificities, and each of the branches on one end

part of the probe is provided with a different detectable function.

21. A circularizable probe having two free nucleic acid end parts which are at least partially complementary to and capable of hybridizing to two at least substantially neighboring regions of a target sequence, wherein or both of the two free nucleic acid end parts of the probe are branched, especially bifurcated.

WO 97/41254